The Lysosome

The lysosome is the one cell organelle that came to prominence in the early years of cell biology that had no direct roots in classical cytology.[39] Rather, Christian de Duve discovered it in the course of research he began in 1949, when he assumed directorship of what he characterized as "the derelict laboratory associated with the Chair of Physiology at the University of Louvain," directed at isolating glucose-6-phosphatase in liver through differential centrifugation. He became interested in glucose-6-phosphatase the previous year, which he spent with Carl and Gerty Cori at Washington University.[40] The Coris had been investigating glucose metabolism and had discovered in liver a hexose phosphatase. Working with liver extracts, de Duve identified the hexose phosphatase as a specific glucose-6-phosphatase and differentiated it from acid phosphatase. When he precipitated the glucose-6-phosophatase in an acid solution, he found he could not redissolve it when he raised the pH level. De Duve had learned from Claude[41] that his large fraction would agglutinate at acid pHs. This suggested to de Duve that agglutination, not precipitation, was occurring in his glucose-6-phosphatase preparations – the enzyme was attached to a structure. He then turned to cell fractionation (helped in part by Claude, who had moved back to Belgium after leaving the Rockefeller Institute) as a gentler way of separating the enzyme than the Waring blender that he had been using, and localized 95% of its activity in the microsomal fraction. What caught de Duve's attention, though, was the fact that the homogenate he prepared before fractionation exhibited only 10% of the acid

[39] In part this is due to the fact it was first identified through its function, not its cytological structure, which Novikoff (1970, p. 121) identified as unusual: "Historically, study of organelles begins usually with the accumulation of morphological observations and then passes to the isolation of the organelle in relatively pure fraction and biochemical study. For lysosomes, however, this pattern was reversed."

[40] Before going to the Coris' laboratory, de Duve had spent eighteen months in Hugo Theorell's laboratory in Sweden where he mastered biochemical techniques. He was interested in visiting the Coris because his earlier research indicated that they had incorrectly ascribed to insulin actions that were not due to insulin itself but to glucagon, a contaminant in their preparations. Carl Cori initially rejected de Duve's request to spend six months in their laboratory but shortly thereafter Earl Sutherland, a postdoctoral fellow in the Coris' laboratory (who later won a Nobel Prize for the discovery of cyclic AMP), obtained evidence that glucagon was the responsible agent. Cori invited de Duve to come and collaborate with Sutherland, which de Duve was able to do with support from the Rockefeller Foundation. The identification of impurity in insulin also paid off handsomely for de Duve. He had determined that insulin prepared by Eli Lilly bore the glucagon contaminant and for alerting them to this fact, the company provided de Duve's laboratory at Louvain with a $5,000/year research budget (Interview with Christian de Duve, 5 December 1995, Rockefeller University, New York).

[41] On his return from St. Louis, de Duve had stopped to visit Claude at the Rockefeller Institute; he reports reading several of Claude's papers on the flight back from New York.

https://doi.org/10.1017/CBO9781139164962.007 Published online by Cambridge University Press